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Closer to clarity on the effect of lipid consumption on fat-soluble vitamin and carotenoid absorption: do we need to close in further?

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Orange, red, yellow, and dark-green vegetables serve as important sources of a number of dietary bioactive phytochemicals, vitamins, and minerals, including 3 of 4 fat-soluble vitamins (FSVs): vitamins E and K and pro-vitamin A carotenoids (1). Indeed, according to the 2015–2020 Dietary Guidelines for Americans (DGA), "Healthy eating patterns include a variety of vegetables from all of the 5 vegetable subgroups—dark green, red and orange, legumes (beans and peas), starchy, and other. These include all fresh, frozen, canned, and dried options in cooked or raw forms, including vegetable juices. The recommended amount of vegetables in the Healthy U.S.-Style Eating Pattern at the 2,000-calorie level is 2 1/2 cup-equivalents of vegetables per day" (1).

However, carotenoid bioavailability from raw vegetables, such as spinach and carrots, tends to be low (e.g. β-carotene is generally 5–10%) (2), which suggests that these foods present a unique challenge as a source of FSVs. To exacerbate this, Americans consume fewer than the DGA-recommended servings of vegetables (1), which is particularly concerning for certain groups, such as non-Hispanic black women of child-bearing age and women living in poverty, who have greater odds of vitamin A insufficiency (3). Non–pro-vitamin A carotenoids may also confer other benefits related to chronic disease prevention. Thus, strategies to extract the greatest benefit from whatever vegetables are consumed make sense.

Previous studies have shown that added oil increases carotenoid bioavailability from raw vegetables (2, 4–6). However, the DGA emphasize, "Vegetables should be consumed in a nutrient-dense form, with limited additions such as salt, butter, or creamy sauces" (1). Fortunately, lipid source, be it butter, canola, or soybean oil, is less important in promoting carotenoid absorption from raw vegetables than is lipid mass (6). The DGA indicate, "The recommendation for oils in the Healthy U.S.-Style Eating Pattern at the 2,000-calorie level is 27 g (about 5 teaspoons) per day" (1). So, this leads to the question of how much oil should be consumed with raw vegetables?

In this issue of the Journal, White et al. (7) use a complete crossover design that includes 5 lipid "dose" amounts across a broad and relevant range (0–32 g, 0–7.1 teaspoons) and use linear mixed-effects modeling to show that lipid mass does significantly and linearly increase carotenoid and tocopherol absorption. Although the current findings are similar to those in previous studies (4–6), there is a key difference. Whereas White et al. found a linear response from 0 to 32 g oil for α-carotene, lycopene, phylloquinone, and retinyl palmitate; 0–8 g for β-carotene; and 0–4 g for lutein, α-tocopherol, and total tocopherol, previous studies were not designed to, and consequently did not, show linear responses across a broad range (5, 6). This clear demonstration also provides nuance to the highly cited finding by Roodenburg et al. (8), which suggested that 3 g added lipid conferred maximal carotene and tocopherol absorption. The study by Roodenburg et al. was conducted with isolated FSVs and carotenoids dissolved in an experimental lipid spread, so in context of the current findings, it becomes clear that the absorption of isolated FSVs and carotenoids solubilized in oil is not representative of bioavailability from plant material.

Another principle shown by White et al. (7) is the between-individual concordance for the absorption of different FSVs and carotenoids, such that high absorbers of one compound tended to be high absorbers of another. This supports the strengthening hypothesis that similar processes dictate FSV and carotenoid absorption (9, 10). This work also indicates that, relative to the carotenoids, the tocopherols are absorbed more efficiently, perhaps due to greater solubility or because they are not metabolized in the gut epithelium as are carotenoids (11). Alternatively, phylloquinone absorption heterogeneity was observed, with 4 of 12 subjects showing clearly increased phylloquinone absorption with increasing oil dose, whereas the others had minimal responses. Perhaps this segregation is due to differences in microbial conversion of phylloquinone to menaquinones of varying

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bioavailability (12), although this study was not designed to test this hypothesis.

As with any controlled study, limitations naturally emerge. First, the subjects studied were young, healthy, normal-weight (race-ethnicity and nutritional status were unknown) women, so the responses may differ with different subject characteristics. Second, the combination of natural plant foods allows for potential interactions between the FSVs and carotenoids, which may affect absorption. Third, we cannot directly extrapolate the effects of lipid co-consumption on the absorption of FSVs and carotenoids from vegetables prepared in a different manner (e.g., cooked, frozen, dried, or chopped). Last, although the report showcases interindividual variation in carotenoid and FSV absorption, it cannot explain its causes. A number of studies have found that a marked proportion of the variability in carotenoid and FSV absorption can be explained by genetic variation among other host-related factors (9, 11), which justifies future research on such modulators.

How can researchers leverage these findings? For one, a raw vegetable–borne carotenoid or tocopherol intervention should include oil or be consumed with a lipid-containing meal. Second, population scientists interested in precisely studying dietary carotenoid and tocopherol exposures and disease risk could develop innovative methods to query and analyze subjects' lipid consumption with plant sources of these compounds.

So, how much oil should your salad dressing provide? These findings suggest merit in adding oil to a raw vegetable salad, with enhanced absorption with low-fat (4 g) and standard (8 g) oil dressings (7), which could fit within the DGA's recommendations (1). Because this study did not engage techniques necessary to estimate FSV and carotenoid masses absorbed, such as physiologic compartmental modeling of absorption from intrinsically labeled vegetables, we cannot yet define how much lipid is necessary to absorb targeted FSV amounts needed to meet the Recommended Dietary Allowance. Furthermore, for personalized nutritional recommendations for risk reduction in specific diseases and conditions to someday become a reality, the continuum from intake to internal exposure to health outcome first must be more precisely understood.

In summary, the study by White et al. is the kind of careful study design with complementary statistics that needs to be done to precisely define the effects of different key variables on FSV and carotenoid absorption. Clearly, bioavailability and the resultant internal exposures are complicated by many variables, but this report makes a significant stride in clarifying one of them.

NEM and EJJ wrote the manuscript; and NEM had primary responsibility for the final content. Neither of the authors had a conflict of interest to declare.

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